

SUPPLEMENTARY DATA

Supplementary Table S1. Clinical Characteristics of the DCCT/EDIC Cohort*

| Characteristics | DCCT at Baseline (1983 – 1989) | | End of DCCT (1993) | | Year 11 of EDIC [†] (2004) | | Year 19/20 of EDIC ^{***} (2012/2013) | |
|-----------------------------------|-----------------------------------|--------------------------------------|-----------------------------------|--------------------------------------|--|--------------------------------------|--|--------------------------------------|
| | Intensive Treatment (N=711) | Conventional Treatment (N=730) | Intensive Treatment (N=698) | Conventional Treatment (N=723) | Intensive Treatment (N=593) | Conventional Treatment (N=589) | Intensive Treatment (N=630) | Conventional Treatment (N=607) |
| Death (N) | 0 | 0 | 7 | 4 | 17 | 28 | 47 | 67 |
| Age (yr) | 27 ± 7 | 27 ± 7 | 34 ± 7 | 33 ± 7 | 46 ± 7 | 45 ± 7 | 55 ± 7 | 54 ± 7 [§] |
| Female sex (%) | 49 | 46 | 49 | 46 | 48 | 46 | 50 | 46 |
| Secondary cohort (%) | 51 | 48 | 51 | 48 | 51 | 48 | 52 | 48 |
| Duration of diabetes (yr) | 6 ± 4 | 5 ± 4 | 12 ± 5 | 12 ± 5 | 24 ± 5 | 23 ± 5 | 33 ± 5 | 32 ± 5 [§] |
| Current cigarette smoker (%) | 19 | 18 | 20 | 20 | 14 | 11 | 11 | 10 |
| Body-mass index | 23.3 ± 2.7 | 23.4 ± 2.9 | 26.6 ± 4.3 | 25.0 ± 3.1 [‡] | 28.2 ± 4.9 | 27.6 ± 4.5 | 29.0 ± 5.6 | 28.4 ± 5.2 |
| Blood pressure (mm Hg) | | | | | | | | |
| Systolic | 113 ± 12 | 115 ± 12 [§] | 117 ± 12 | 117 ± 12 | 120 ± 14 | 121 ± 15 | 121 ± 16 | 121 ± 15 |
| Diastolic | 72 ± 9 | 73 ± 9 | 75 ± 9 | 74 ± 9 | 75 ± 9 | 75 ± 9 | 70 ± 10 | 70 ± 9 |
| Hypertension (%) [¶] | 0 | 0 | 4 | 4 | 50 | 54 | 68 | 70 |
| Lipids [‡] | | | | | | | | |
| HDL cholesterol (mg/dl) | 51 ± 12 | 50 ± 12 | 51 ± 13 | 52 ± 13 | 54 ± 15 | 54 ± 15 | 63 ± 21 | 61 ± 18 |
| LDL cholesterol (mg/dl) | 110 ± 29 | 109 ± 29 | 112 ± 27 | 115 ± 32 | 110 ± 30 | 105 ± 28 [§] | 98 ± 30 | 95 ± 30 [§] |
| Total cholesterol (mg/dl) | 177 ± 33 | 176 ± 34 | 180 ± 31 | 184 ± 38 | 182 ± 34 | 176 ± 33 [‡] | 177 ± 36 | 172 ± 39 [‡] |
| Triglycerides (mg/dl) | 81 ± 43 | 82 ± 51 | 84 ± 53 | 88 ± 51 [§] | 92 ± 65 | 84 ± 57 [§] | 82 ± 54 | 81 ± 63 |
| Hyperlipidemia (%) ^{**} | 0 | 0 | 26 | 30 | 53 | 48 | 68 | 66 |
| Renal function ^{#,††} | | | | | | | | |
| Albumin excretion rate (mg/24 hr) | 16.4 ± 19.6 | 15.5 ± 17.9 | 29.8±197.6 | 75.4±441.1 [‡] | 62.8±429.9 | 96.8±474.1 [§] | 89.6±420.9 | 118.5±530.3 |
| Albuminuria | | | | | | | | |

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| | | | | | | | | |
|--|-----------------|-----------------|-----------------|------------------------------|-----------------|------------------------------|-----------------|------------------------------|
| Sustained Microalbuminuria (Sustained AER ≥ 30 or ESRD) (%) | 5 | 4 | 8 | 15 [‡] | 10 | 18 [‡] | 13 | 20 [‡] |
| Macroalbuminuria (AER ≥ 300 or ESRD) (%) | 0 | 0 | 1 | 3 [§] | 3 | 7 [‡] | 5 | 9 [§] |
| Kidney failure (eGFR < 15 ml/min per 1.73 m ² or ESRD) (%) | 0 | 0 | 0 | 0 | 0.7 | 1.0 | 1.3 | 2.5 |
| HbA1c (%) | 9.1 \pm 1.6 | 9.1 \pm 1.6 | 7.4 \pm 1.2 | 9.1 \pm 1.6 [‡] | 7.9 \pm 1.3 | 7.8 \pm 1.3 | 8.0 \pm 1.2 | 8.0 \pm 1.2 |
| mmol/mol | 75.8 \pm 17.4 | 75.5 \pm 17.9 | 57.6 \pm 12.7 | 76.4 \pm 17.0 [‡] | 62.5 \pm 14.0 | 61.7 \pm 13.8 | 64.3 \pm 13.6 | 63.8 \pm 13.0 |
| Time-weighted Mean HbA1c (%) | — | — | 7.3 \pm 0.9 | 9.1 \pm 1.3 [‡] | 7.7 \pm 0.9 | 8.4 \pm 1.0 [‡] | 7.8 \pm 0.9 | 8.2 \pm 0.9 [‡] |
| mmol/mol | — | — | 56.3 \pm 10.1 | 75.8 \pm 13.7 [‡] | 60.4 \pm 10.3 | 68.3 \pm 10.9 [‡] | 61.4 \pm 10.0 | 66.3 \pm 10.1 [‡] |
| Heart rate (beats/min) | 68 \pm 11 | 68 \pm 11 | 69 \pm 12 | 71 \pm 12 [‡] | 68 \pm 11 | 70 \pm 11 [§] | 68 \pm 11 | 69 \pm 11 |
| Medication (%) ^{‡‡} | | | | | | | | |
| ACE inhibitors or ARBs (for any cause) | — | — | — | — | 41 | 46 | 57 | 60 |
| Hormone-replacement therapy | — | — | — | — | 16 | 14 | 10 | 8 |
| ≥ 14 Aspirin tablets/mo | — | — | — | — | 39 | 44 | 56 | 56 |
| Beta-blocker | — | — | — | — | 4 | 8 [‡] | 13 | 15 |
| Statin | — | — | — | — | 36 | 37 | 56 | 56 |
| Intensive diabetes management ^{§§} | 0 | 0 | 98 | 5 [‡] | 97 | 94 [§] | 98 | 98 |

* Plus-minus values are means \pm SD. HDL denotes high-density lipoprotein, LDL low-density lipoprotein, ACE angiotensin-converting enzyme, and ARB angiotensin-receptor blocker. The body-mass index is the weight in kilograms divided by the square of the height in meters. To convert values for cholesterol to millimoles per liter, multiply by 0.02586. To convert values for triglycerides to millimoles per liter, multiply by 0.1129.

[†] The annual EDIC examination at year 11 was completed for 1182 of the surviving patients at the time of data closeout for this study.

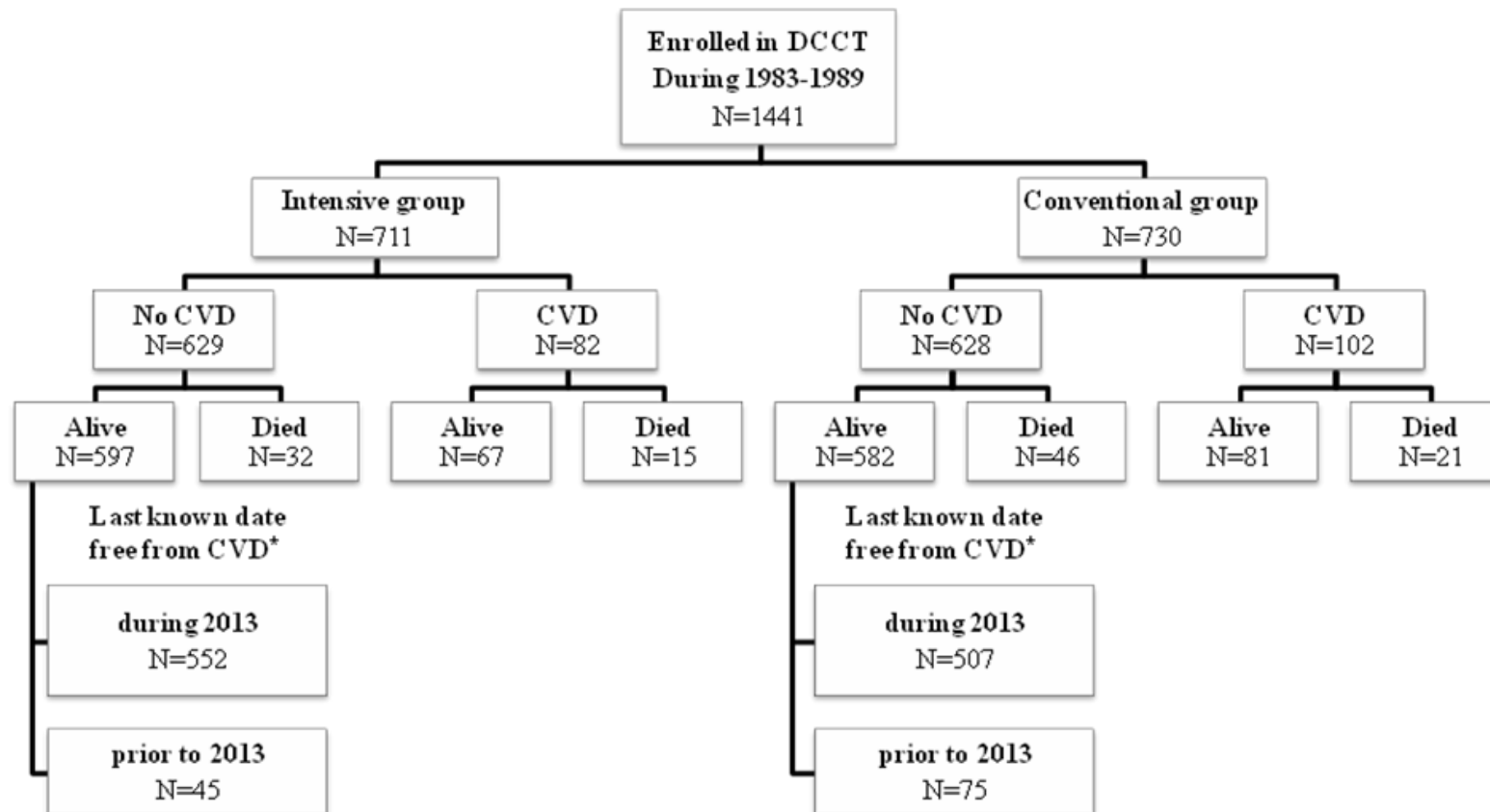
[‡] P<0.01 by the Wilcoxon rank-sum test or the chi-square test comparing conventional and intensive treatment.

[§] P<0.05 by the Wilcoxon rank-sum test or the chi-square test comparing conventional and intensive treatment.

[¶] Hypertension was defined by a systolic blood pressure of at least 140 mm Hg, a diastolic blood pressure of at least 90 mm Hg, documented hypertension, or the use of antihypertensive agents.

SUPPLEMENTARY DATA

Supplementary Figure S1. Number of Patients with/without Any Cardiovascular Disease (CVD) during DCCT/EDIC by Treatment Group



* 1059 (552 + 507) subjects had nearly complete follow-up, 434 of these were known to be free of CVD on the data lock date of 12/31/13 and thus represent 100% complete follow-up. 120 (45+75) subjects were last known to be free of CVD more than a year prior to the closeout date.